

Amendment to the specification:

Please replace the paragraph beginning at page 4, line 12, with the following paragraph:

-- In a particularly preferred embodiment the enzyme is a *Bacillus lentus* subtilisin. In preferred embodiments, the cysteine is substituted for an amino acid in a subtilisin, where the amino acid corresponds to a reference residue in a *Bacillus lentus* subtilisin (Protein Accession number P29600), where the reference residue is at or near a residue selected from the group consisting of residue 156, residue 166, residue 217, residue 222, residue 62, residue 96, residue 104, residue 107, residue 189, and residue 209.

Please replace the paragraph beginning at page 11, line 32 with the following paragraph:

--The conserved residues may be used to define the corresponding equivalent amino acid residues in other related enzymes. For example, the two (reference and "target") sequences are aligned in order to produce the maximum homology of conserved residues. There may be a number of insertions and deletions in the "target" sequence as compared to the reference sequence. Thus, for example, a number of deletions are seen in the thermitase sequence as compared to *B. amyloliquefaciens* subtilisin (Protein Accession number CAA24990) (see, e.g. U.S. Patent 5,972,682). Thus, the equivalent amino acid of Tyr217 in *B. amyloliquefaciens* subtilisin in thermitase is the particular lysine shown beneath Tyr217 in Figure 5B-2 of the 5,972,682 patent.--

Please replace the paragraph beginning at page 44, line 8 with the following paragraph:

--In a preferred embodiment, however, residues for modification/substitution in the enzyme (e.g. serine hydrolase) are rationally selected. Preferred sites include sites not in critical conformation determining regions and sites disposed away from the subsite(s) of the enzyme. However, in other preferred embodiments, particularly where it is desired to enhance, or otherwise alter, substrate specificity and/or activity, preferred amino acid residues selected for modification include residues expected to be important discriminatory sites near, adjacent to or within the substrate binding region of the enzyme. Such residues are determined from mutagenesis experiments where the subsite residues are systematically mutagenized and the effect of such mutagenesis on binding specificity and/or enzymatic activity is determined. In addition, important residues can be identified from inspection of crystal structures of the enzyme alone or in

complex with substrate, substrate analogues or inhibitors and/or from predicted protein folding or protein-protein interactions determined using protein modeling software (*e.g.*, Quanta, Cerius, Insight (Molecular Simulations Inc.) and Frodo (academic software). Side chains situated to alter interaction at subsites defined by Berger and Schechter can be selected based on the crystallographic models of the enzymes and extrapolated to homologous enzymes if necessary if structural information on a specific enzyme is unavailable. In *B. lentus* subtilisin (Protein Accession Number P29600) sites 62, 156, 166, 217 and 222 are important substrate specificity determining sites. Additional related sites include position 96, 104, 107, 189 and 209 in subtilisin and homologous positions in related enzymes. In preferred embodiments, such residues typically lie in the S1, S2, S4, S1', S2', or S3' subsites although it will be appreciated that in certain cases, alteration of residues in other subsites can also produce dramatic effects.--